

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER see Notification (Form PCT/ISA/2	of Transmittal of International Search Report 220) as well as, where applicable, item 5 belo
ABL-012-PCT International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/BE 03/00192	07/11/2003	08/11/2002
Applicant		
ABLYNX N.V.		
This International Search Report has been according to Article 18. A copy is being tra	n prepared by this International Searching Auth Ansmitted to the International Bureau.	nority and is transmitted to the applicant
-This International Search-Report consists	of a total ofsheets	in the state of th
X It is also accompanied by	a copy of each prior art document cited in this	report.
Basis of the report      With regard to the language, the i	nternational search was carried out on the bas	is of the international application in the
language in which it was filed, unle	ess otherwise indicated under this item.	
Authority (Rule 23.1(b)).	as carried out on the basis of a translation of th	
<ul> <li>With regard to any nucleotide and was carried out on the basis of the</li> </ul>	I/or amino acid sequence disclosed in the integration in the integration is sequence listing:	ernational application, the international searc
	nal application in written form.	
filed together with the inter	national application in computer readable form	•
<del>L</del>	his Authority in written form.	
_	his Authority in computer readble form.	
international application as		
x the statement that the information furnished	mation recorded in computer readable form is i	dentical to the written sequence listing has be
		*
2. X Certain claims were found	d unsearchable (See Box I).	
3. Unity of invention is lacki	ng (see Box II).	
4. With regard to the title,	mitted by the applicant	
X the text is approved as subjects	ed by this Authority to read as follows:	
the text has been established	by this Authority to read as lonowe.	
5. With regard to the abstract,		·
the text is approved as subr	nitted by the applicant.	
the text has been established within one month from the d	ed, according to Rule 38.2(b), by this Authority ate of mailing of this international search repor	as it appears in Box III. The applicant may, t, submit comments to this Authority.
6. The figure of the drawings to be publish	ned with the abstract is Figure No.	
as suggested by the applica	nt.	X None of the figures.
because the applicant failed	to suggest a figure.	
hanning this figure hotter of	earacterizes the invention	





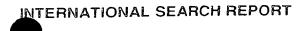
International application No.

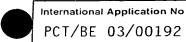
PCT/BE 03/00192

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to polypeptides derived from single domain heav hain antibodies directed to Tumor Necrosis Factor-alpha. It further relates tingle domain antibodies that are Camelidae VHHs. It further relates to method f administering said polypeptides.

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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07K16/28 C07K16/18

A61P37/06 G01N33/577

CO7K16/46 A61P19/02

A61K39/395

C12N15/13

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K C07K IPC 7

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	WO 91/02078 A (PEPTIDE TECHNOLOGY LTD) 21 February 1991 (1991-02-21) page 3, line 28 -page 4, line 24	1
Y	page 15, line 25 - line 33	2-49
Y	ELS CONRATH K ET AL: "Camel single-domain antibodies as modular building units in bispecific and bivalent antibody constructs" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 276, no. 10, 9 March 2001 (2001-03-09), pages 7346-7350, XP002248402 ISSN: 0021-9258 the whole document	2-49

Further documents are listed in the continuation of box C.	Patent family members are listed in annex.		
* Special categories of cited documents:  *A* document defining the general state of the art which is not considered to be of particular relevance  *E* earlier document but published on or after the international filing date  *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	<ul> <li>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</li> <li>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</li> <li>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the</li> </ul>		
<ul> <li>O* document referring to an oral disclosure, use, exhibition or other means</li> <li>P* document published prior to the international filling date but later than the priority date claimed</li> </ul>	document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  *&* document member of the same patent family		
Date of the actual completion of the international search	Date of mailing of the international search report		
7 May 2004	14/05/2004		
Name and mailing address of the ISA	Authorized officer		
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Le Flao, K		





International Application No PCT/BE 03/00192

	C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
	Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Y	VALLE E ET AL: "Infliximab" EXPERT OPINION ON PHARMACOTHERAPY, ASHLEY, LONDON,, GB, vol. 2, June 2001 (2001-06), pages 1015-1025, XP002965315 ISSN: 1465-6566 the whole document	1-49
	Y	WO 02/057445 A (MURUGANANDAM ARUMUGAM;STANIMIROVIC DANICA (CA); NARANG SARAM (CA)) 25 July 2002 (2002-07-25) page 18, line 29 -page 47, line 18	1-49
	A	WO 02/079781 A (ANDREWS JANET S; HESKA CORP (US); JENSEN WAYNE A (US); MCDONALD TH) 10 October 2002 (2002-10-10) page 26, line 25 -page 28, line 21 page 29, line 14 - line 20	4
BEST AVAILABLE COPY	A	TANHA J ET AL: "Selection by phage display of llama conventional VH fragments with heavy chain antibody VHH properties" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER, AMSTERDAM, NL, vol. 263, no. 1-2, 1 May 2002 (2002-05-01), pages 97-109, XP004354388 ISSN: 0022-1759 the whole document	1-49
E COPY	A	D'HAENS G ET AL: "ENDOSCOPIC AND HISTOLOGICAL HEALING WITH INFLIXIMAB ANTI-TUMOR NECROSIS FACTOR ANTIBODIES IN CROHN'S DISEASE: A EUROPEAN MULTICENTER TRIAL" GASTROENTEROLOGY, SAUNDERS, PHILADELPHIA, PA, US, vol. 116, no. 5, May 1999 (1999-05), pages 1029-1034, XP009009036 ISSN: 0016-5085 the whole document	1-47
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## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 22-24

Present claims 22-24 relate to a product defined by reference to a desirable characteristic or property, namely "an unknown agent that modulates the binding of an anti-TNF-alpha polypeptide of any of claims 1 to 11, and 13 to 16 to Tumor Necrosis Factor-alpha" (claim 22) and "an unknown agent that modulates Tumor Necrosis Factor-alpha-mediated disorders" (claim 23). The scope of claims 22-24 is unclear and speculative within the meaning of Article 6 PCT. Said claims lack indication concerning their technical features. The available experimental data actually relate to anti-TNF-alpha single domain antibodies and their preparation, but not to an agent that modulates their binding. Consequently no search has been carried out for the claims 22-24.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT



International application No. PCT/BE 03/00192

	Box 1 Observations where certain ordinary trees to the contraction of
	This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	2. X Claims Nos.: 22-24 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  See FURTHER INFORMATION sheet PCT/ISA/210
	3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
7	Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
FOT AVAILABLE	This International Searching Authority found multiple inventions in this international application, as follows:
3LE Q	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
A.A.O	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
	3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
	Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

Information on patent family members



International Application No PCT/BE 03/00192

Patent document cited in search report	Publication date		Patent family member(s)		Publication date	
WO 9102078 A	21-02-1991	AU WO EP CA DE DE DE US US US US	9102078 0486526 2064915 69027121 69027121 486526 3443119 2003096096 2003231699 2003162948 2003232970 2004002588	A A1 A1 D1 T2 T3 B2 A A1 A1 A1	26-08-199 11-03-199 21-02-199 27-05-199 08-02-199 27-06-199 14-11-199 24-06-199 02-09-2003 19-08-2003 18-12-2003 01-01-2004 11-09-2003 20-11-2003	91 91 92 16 66 63 33 33 43 33
		US US US US US US US US US US US	2004002589 A	A1 A1 A1 A1 A1 A1 A1 A1 A1 A1 A1	01-01-2004 06-11-2003 01-07-1997 11-09-2003 11-09-2003 01-01-2004 04-12-2003 09-07-2002 18-12-2003 15-07-2003 30-08-2001 20-09-2001 30-08-2001	<b>1 3 </b>
WO 02057445 A	25-07-2002	AU WO WO CA CA	6885501 A 0190190 A 02057445 A 2380443 A 2441903 A	2 1 1 1	03-12-2001 29-11-2001 25-07-2002 29-11-2001 25-07-2002	
		EP - US	1328626 A12003190598 A1		23-07-2003 09-10-2003	
WO 02079781 A	10-10-2002	CA EP WO US	2442074 A3 1384075 A3 02079781 A3 2003022262 A3	1 1	10-10-2002 28-01-2004 10-10-2002 30-01-2003	